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Other titles: Idiopatická cystitida a infekce močových cest u koček

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Idiopathic cystitis and urinary tract infection

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Abstract

Idiopathic cystitis and urinary tract infections are diseases of cats included in the term feline lower urinary tract disease. While urinary tract infection is well defined, mostly diagnosable and can often be cured with adequate treatment, idiopathic cystitis remains an unclear syndrome. Idiopathic cystitis is diagnosed by exclusion and no treatment has consistently been successful in against this disease.

Introduction

Diseases of the lower urinary tract of cats are summarized under the term “Feline Lower Urinary Tract Disease” FLUTD. FLUTD describes the common clinical presentation of different diseases with a wide variety of causes. The signs of FLUTD are pollakiuria (frequent voiding of small amounts of urine), stranguria (painful, not controllable micturation), periuria (urination in inappropriate places) and hematuria. (Westropp and Buffington 2010). Obstruction of the urethra may or may not occur. FLUTD is a common problem in veterinary medicine. Investigations in the USA revealed that 8% of the cats presented to teaching hospitals suffered from FLUTD (Lekcharoensuk et al 2001).

If the cause of FLUTD can not be identified the disease is called idiopathic. In a recent study from Norway 56% of cats with FLUTD suffered from idiopathic cystitis, 21% had urethral plugs, 12% urolithiasis, and 12% a urinary tract infection (Sævik et al 2011). In an earlier study at our hospital the numbers were very similar. 58% of the cats with FLUTD suffered from idiopathic cystitis, 10% had urethral plugs, 22% had urinary calculi, and 8% urinary tract infections (Gerber et al 2005). Further less common causes of FLUTD are neoplasias (e.g. transitional cell carcinoma), acquired or congenital anatomic defects, and central nervous system diseases leading to micturation disturbances.

Because all forms of FLUTD have the same clinical presentation, diagnostic imaging and laboratory tests are essential in each case to establish a diagnosis.

Radio dense stones can be seen on radiographs, furthermore size and form of the bladder can be evaluated. It is important to make sure that the distal end of the urethra is on the radiograph. Ultrasound evaluation of the urinary tract provides information about the bladder wall and the content of the bladder. Hyperechogenic floating material is often seen on ultrasound, however similar findings can be seen in healthy cats. Diseases of the urethra can be detected by contrast urethrography or computetd tomography (CT). CT also provides insight in the upper urinary tract. Urethroscopy and cystoscopy might be performed in selected cases.

Urinalysis is very important and urine should always be collected before any therapy is started. Therapy could potentially change the urinalysis results and lead to the wrong diagnosis. Ideally urine should be collected by cystocentesis; however there is some debate about the danger of cystocentesis in obstructed cats. Urinalysis should include measurement of the specific gravity, a dip-stick analysis, analysis of the urine sediment and a urine culture. For the interpretation of results of the urinalysis it is important to remember that crystalluria is not a disease. Serum biochemical analysis can provide information about underlying diseases. For example hypercalcemia can lead to the formation of calcium-oxalate stones or cats with diabetes mellitus might be more prone to urinary tract infections. Furthermore it is important to identify and quantify hyperkalemia or postrenal azotemia in cats with urinary tract obstruction. Postrenal azotemia develops about 24 h after the obstruction of the urethra. Electrolyte disturbances specifically hyperkalemia can be life threatening and should be treated immediately.

Idiopathic cystitis

It is unknown what is causing idiopathic cystitis. A still unproven hypothesis was the involvement of infectious agents since injection of urine from affected cats into the urinary bladders of unaffected cats caused urethral obstruction (Rich and Fabricant 1969). Caliciviruses isolated from a cat with urinary tract obstruction caused the same signs in other cats inoculated with this virus. However these experiments were not reproducible leaving the question open, if viruses are truly involved in the development of idiopathic cystitis. Defects in the glycosaminoglycan layer and therefore higher permeability of the bladder epithelium, increased activity of the sympathetic nervous system and neurogenic inflammation seem to be features of the disease (Westropp and Buffington 2010).

In one study risk factors associated with idiopathic cystitis were male gender, overweight, pedigree cat and most importantly living with another cat with which there was conflict (Cameron et al 2004). This implies that stress might be a trigger for the disease, which is supported by the finding that bladder permeability in cats with idiopathic cystitis is highest under stress (Westropp et al 2006). However it was suspected that not demographic or environmental factors but rather cat-related factors like timidity were associated with idiopathic cystitis (Buffington et al 2006). Idiopathic cystitis occurs rather in young to middle aged cats, if obstructive males are overrepresented (Westropp and Buffington 2010).

Cats suffering from idiopathic cystitis show pain, hematuria, pollakiuria, stranguria, periuria or are not able to urinate at all. This picture is not different from other causes of FLUTD. In our patients expression of pain, hematuria, pollakiuria, or stranguria were seen in about 50% of the cases with idiopathic cystitis while periuria was seen in only 35%. More than half of the cats (55%) were presented with urethral obstruction, however urethral plugs could not be ruled out in these cats (Gerber et al 2005).

If the cats urethra is obstructed an emergency treatment is required. The goal of the therapy is to re-establish urine flow. Life threatening metabolic abnormalities like hyperkalemia or severe acidosis must be corrected immediately. About 12% of cats with urethral obstruction were found to have severe hyperkalemia (>8mmol/l) (Lee et al 2003). Possibilities for the therapy of hyperkalemia are: -infusion with NaCl 0.9%; -infusion with glucose 5%; -regular insulin (0.2 IU/kg IV) followed by a glucose bolus (2 g glucose per unite insulin) followed by infusion with glucose 5%; -calcium gluconate 10%, 0.5 – 1.5 ml/kg IV over 10 minutes; -sodium bicarbonate 0.2 – 0.5 mmol/kg with infusion. Decompressive cystocentesis can be performed if immediate relief of the obstruction is not achieved. Possible side effects of this procedure are extravasation of urine into the peritoneal cavity and injury to a pre damaged bladder wall, therefore it is not recommended as routine procedure. Once the urethra is patent we prefer to leave an indwelling catheter in place and connected to a closed urine collecting system. After severe postrenal azotemia a substantial post obstructive diuresis might occur and should be addressed by adequate infusion.

If other reasons are excluded idiopathic cystitis can be suspected. Many cats with idiopathic cystitis recover spontaneously. A specific therapy has not been established so far. Different medications and treatments have been recommended, however they remained tentative and many relapses are seen. Controlled studies proofing the efficacy of treatments are lacking.

In humans idiopathic cystitis is also classified as a chronic pain syndrome, indicating that pain is an important part of the disease. Pain seems to be a common feature of idiopathic cystitis and should therefore be addressed. Changes of the glycosaminoglycan layer of the bladder seem to occur in idiopathic cystitis. Therefore it seems logic to replace glycosaminoglycans. In humans some success was described, however the success was not consistent. In veterinary medicine one study showed no difference between cats treated with N-acetyl glucosamine for six month compared to cats treated with a placebo (Gunn-Moore and Shenoy 2004).

Amitriptyline is a tricyclic antidepressant and is used in veterinary medicine for behavioral problems. Amitriptyline is thought to have antihistaminic, anticholinergic, anti-alpha-adrenergic, anti inflammatory, analgetic und mild sedative actions. Based on this broad spectrum of action amitriptyline seemed to be ideal for the treatment of all forms of FLUTD. In humans the medication provided some relief in patients with interstitial cystitis. In two veterinary studies amitriptyline was used for a short period of time in cats with idiopathic FLUTD.(Kraijer et al 2003; Kruger et al 2003). In both studies no positive effect of the medication could be demonstrated. In another unfortunately uncontrolled study amitriptyline lead to a reduction of clinical signs in 9 of 15 cats which were treated for one year (Chew et al 1998).
Signs of idiopathic cystitis may be exacerbated by stress (Westropp et al 2006) and adaptation of the cat's environment might reduce stress (Buffington et al 2006). Pheromones are thought to reduce stress in cats. In a pilot study synthetic feline facial pheromones (Feliway®) were used for the treatment of idiopathic cystitis (Gunn-Moore et al 2004). No significant difference was seen between treated and untreated cats.
The recurrence rate in cats receiving a diet in canned form was lower than in cats receiving the same diet in dry form (Markwell et al 1999). Furthermore improvement of clinical signs in cats with idiopathic cystitis was attributed to the change on a canned diet in one study (Gunn-Moore et al 2004). This implies that adding water in the diet might be beneficial for cats with idiopathic cystitis.
Prognosis in non obstructive idiopathic cystitis is not known. In two studies the prognosis obstructive idiopathic cystitis was guarded (Gerber et al 2008; Segev et al 2010). Recurrence of obstruction was 36% and 24% respectively. Other signs of lower urinary tract disease were common in one of the studies (Gerber et al 2008).

Urinary tract infection
Urinary tract infections (UTI) can occur either in the upper or the lower urinary tract or in both sites at once. It might sometimes be difficult to detect the location of an infection. Furthermore an infection in one part of the urinary tract increases the likelihood of another part of the urinary tract becoming infected as well. Most UTIs are the result of ascending migration of pathogens from the distal urogenital tract to the sterile part (Pressler and Bartges 2010). UTI develops when the host's defenses are overwhelmed by microbes. Normal defenses include wash-out of pathogens by normal micturation with complete emptying of the bladder, mucosal layer with glycosaminoglycanes, epithelial desquamation, functional properties like ureteral peristalsis and local and systemic immune competence. Furthermore urine itself has antimicrobial properties that may play a role in limiting bacterial growth and include high osmolality, urine constituents with antimicrobial effect (e.g. high concentration of urea, organic acids, Tamm-Horsfall mucoproteins or low-molecular weight carbohydrates) and extreme values of urine pH (Osborne and Lees 1995).
UTIs in cats are less common than in dogs. They account for around 10% of the cats with signs of FLUTD (Gerber et al 2005; Sævik et al 2011). However in one study one third of the cats with FLUTD showed bacteriuria (Eggertsdóttir et al 2007). *Escherichia coli* is the most common isolate cultured from urine followed by gram-positive cocci (Pressler and Bartges 2010). Fungal UTI are mostly associated with underlying urinary tract or medical diseases (Jin and Lin 2005). In one study 0.4% of the UTIs were caused by viruses, however the viruses involved were not specified (Lekcharoensuk et al 2001).
Older cats (10 years+) have shown an increased risk of getting UTI while in cats less than 1 year, the risk is minimal and female spayed cats had an increased risk of bacterial UTI while female and male intact cats showed a decreased risk for bacterial UTI (Lekcharoensuk et al 2001). In the same study Abyssinian cats were at increased risk for UTI.

Underlying conditions like diabetes mellitus, hyperthyreoidism and renal insufficiency increase the risk of UTI in cats (Mayer-Roenne et al 2007). After obstructive LUTD, indwelling catheters with a closed system may cause UTI. However treatment while the catheter is in place is not advisable. Urinalysis with culture and appropriate treatment at the time of removal of the catheter is recommended (Barsanti et al 1992). UTI is the most frequent late complication of perineal urethrostomy (Bass et al 2005).
As in all cats with FLUTD the clinical signs consist of haematuria, pollakiuria, stranguria and urination in inappropriate places also termed periuria. Urethral obstruction is rare. Gross haematuria was more often reported in historical findings in cats later diagnosed as having UTI than in other cats later diagnosed as having other causes for FLUTD (Gerber et al 2005).
Occult bacterial UTIs with no clinical signs can occur in cats particularly in older ones (Litster et al 2009).
The gold standard for diagnosis of UTI is urine culture. Examination of the urine sediment provides some help in the identification of UTI. More than 4 white blood cells per 400X field in an unstained sediment under a cover slip together with bacteria identified during the same examination are indicatives. However the presence of pyuria represents any inflammation and is not synonymous with UTI. The absence of pyuria does not rule out UTI. Rod shaped bacteria might be seen in the sediment if more than 10'000/ml Urine are present. Cocci might not be seen before 100'000 bacteria/ml appear in the urine. The presence of bacteria might represent contamination or amorphous particles resembling bacteria.
Proper handling of the urine after collection is very important and urine should ideally be cultured immediately after sampling because some bacteria may multiply very rapidly while others may decrease in number.
Administration of antimicrobial agents should be based on susceptibility testing. Fortunately most antimicrobials are present in urine in high concentrations as a result of renal excretion. Which means even if an antibiotic is used to which the organism is reported to be resistant a good result may be obtained in an animal that can concentrate the urine. An antimicrobial is said to be effective if the urine concentration reaches four times the minimum inhibitory concentration (MIC). Empirical treatment is often necessary before culture and sensitivity results are available. Antibiotics are chosen based on urine sediment results (cocci or rods). Rods in acidic urine may represent *E. coli* while in alkaline urine they may represent *Proteus spp.* Cocci in acidic urine may represent *Enterococcus spp.* while in alkaline urine *Staphlococcus spp.* is more likely.
Preferably, treatment of UTI in cats should be based on culture and sensitivity testing. Appropriate antibiotics should be given for 10 to 14 days in uncomplicated cases (Pressler and Bartges 2010). Uncomplicated UTIs are those in which no underlying problem is found. Clinical signs should disappear after 48 hours. Reculture of the urine 5 to 7 days after treatment is ended can be done to discover a possible underlying causes of the infection. Special caution is needed with the use of fluorquinolones due to the potential risk for retinal degeneration. As renal impairment is often associated with UTI, it is speculated that with decreased renal function fluorquinolones may accumulate which would require dosage reduction and monitoring for mydriasis (Hostutler et al 2005). Aproximately 85% of UTI in cats are single episodes and do not recur (Ling 2000).
Complicated UTIs are UTIs in animals with identifiable predispositions to UTI (e.g. diabetes mellitus, renal failure). In these animals treatment for a longer period than the routine 10 to 14 days may be indicated (up to 4-6 weeks). In these cases it may also be indicated to test the urine after the first week of treatment to evaluate the response to therapy, and before the end of treatment to make sure that no more bacteria are present before treatment is stopped.
Relapsing UTI might either be caused by the same organism which was isolated before treatment (persistent UTI) or by a different organism (recurrent UTI). In both cases further work is required

to identify the underlying causes. If predisposing disorders are not addressed, control of UTI will be poor. Reasons for poor response to therapy might be treatment of a non infectious problem with antibiotics, infectivity of the antibiotics because of inadequate delivery (poor client compliance, poor patient acceptance, ineffective drug or impaired drug transport), resistant microbes or super infection with another organism. For example super infections can occur when antimicrobials are released while a urinary catheter is in place. Recurrent infections, less than three times a year, can be handled as single episodes of uncomplicated UTI. More frequent episodes should be handled as complicated infections. Prophylactic antimicrobial therapy might be indicated after catheterization. Long-term suppressive therapy is indicated if the patient experiences relapses each time antimicrobial therapy is stopped. This treatment strategy is not well studied in veterinary medicine. Half to a third of the usual therapeutic dose of an antimicrobial is given in the evening. The choice of the antimicrobial is based on the last positive culture and the duration of therapy is at least 6 months. Urinalysis and culture are performed every 4 to 8 weeks.

Literature

Barsanti JA, Shotts EB, Crowell WA, Finco DR, Brown J (1992) Effect of therapy on susceptibility to urinary tract infection in male cats with indwelling urethral catheters. *J Vet Intern Med* **6**(2):64-70.

Bass M, Howard J, Gerber B, Messmer M (2005) Retrospective study of indications for and outcome of perineal urethrostomy in cats. *J Small Anim Pract* **46**(5):227-31.

Buffington CA, Westropp JL, Chew DJ, Bolus RR (2006) Clinical evaluation of multimodal environmental modification (MEMO) in the management of cats with idiopathic cystitis. *J Feline Med Surg* **8**(4):261-8.

Buffington CA, Westropp JL, Chew DJ, Bolus RR (2006): Risk factors associated with clinical signs of lower urinary tract disease in indoor-housed cats. *J Am Vet Med Assoc* **228**(5):722-5.

Cameron ME, Casey RA, Bradshaw JW, Waran NK, Gunn-Moore DA (2004). A study of environmental and behavioural factors that may be associated with feline idiopathic cystitis. *J Small Anim Pract* **45**(3):144-7.

Chew DJ, Buffington CA, Kendall MS, DiBartola SP, Woodworth BE (1998) Amitriptyline treatment for severe recurrent idiopathic cystitis in cats. *J Am Vet Med Assoc* **213**(9):1282-6.

Eggertsdóttir AV, Lund HS, Krontveit R, Sørum H (2007) Bacteriuria in cats with feline lower urinary tract disease: a clinical study of 134 cases in Norway. *J Fel Med Surg* **9**:458-65.

Gerber B, Boretti FS, Kley S, Laluha P, Muller C, Sieber N, Unterer S, Wenger M, Flückiger, Glaus, Reusch CE (2005) Evaluation of clinical signs and causes of lower urinary tract disease in European cats. *J Small Anim Pract* **46**(12):571-77.

Gerber B, Eichenberger S, Reusch CE (2008) Guarded long-term prognosis in male cats with urethral obstruction. *J Feline Med Surg* **10**(1):16-23.

Gunn-Moore DA, Cameron ME (2004) A pilot study using synthetic feline facial pheromone for the management of feline idiopathic cystitis. *J Fel Med Surg* **6**(3):133-8.

Gunn-Moore DA, Shenoy CM (2004): Oral glucosamine and the management of feline idiopathic cystitis. *J Fel Med Surg* **6**(4):219-25.

Hostutler RA, Chew DJ, DiBartola SP (2005) : Recent concepts in feline lower urinary tract disease. *Vet Clin North Am Small Anim Pract* **35**(1):147-70.

Jin Y, Lin D (2005): Fungal Urinary Tract Infections in the dog and cat: A retrospective study (2001-2004). *J Am Anim Hosp Assoc* **41**:373-81.

Kraijer M, Fink-Gremmels J, Nickel RF (2003): The short-term clinical efficacy of amitriptyline in the management of idiopathic feline lower urinary tract disease: a controlled clinical study. *J Feline Med Surg* **5**(3):191-6.

Kruger JM, Conway TS, Kaneene JB, Perry RL, Hagenlocker E, Golombek A, Stuhler (2003): Randomized controlled trial of the efficacy of short-term amitriptyline administration for treatment of acute, nonobstructive, idiopathic lower urinary tract disease in cats. *J Am Vet Med Assoc* **222**(6):749-58.
Lee JA, Drobatz KJ (2003): Characterization of the clinical characteristics, electrolytes, acid-base, and renal parameters in male cats with urethral obstruction. *J Vet Emerg Crit Care* **13**(4):277-33.
Lekcharoensuk C, Osborne CA, Lulich JP (2001) Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Asso* **218**:1429-35.
Lekcharoensuk C, Osborne CA, Lulich JP (2001): Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Assoc* **218**(9):1429-35.
Ling GV. Bacterial infections of the urinary tract (2000). In: Ettinger SJ. Feldman EC. eds. Textbook of Veterinary Internal Medicine. Philadelphia: WB Saunders p 1678-86.
Litster A, Moss S, Platell J, Trott DJ (2009) Occult bacterial lower urinary tract infections in cats-Urinalysis and culture findings. *Vet Microbiol* **136**:130-34
Markwell PJ, Buffington CA, Chew DJ, Kendall MS, Harte JG, DiBartola SP (1999) Clinical evaluation of commercially available urinary acidification diets in the management of idiopathic cystitis in cats. *J Am Vet Med Assoc* **214**(3):361-5.
Mayer-Roenne B, Goldstein RE, Erb HN (2007): Urinary tract infections in cats with hyperthyroidism, diabetes mellitus and chronic kidney disease. *J Fel Med Surg* **9**(2):124-32.
Osborne CA, Kruger JM, Lulich JP. Feline lower urinary tract disorders (1996). Definition of terms and concepts. *Vet Clin North Am Small Anim Pract* **26**:169-79.
Osborne CA, Lees GE (1995) Bacterial infections of the canine and feline urinary tract. In: Osborne CA, Finco DR. eds. Canine and feline nephrology and urology. Baltimore: Williams & Wilkins, p 757-97.
Pressler B, Bartges JW (2010): Urinary tract infection. In: Ettinger SJ, Feldman EC, editors. *Textbook of Veterinary Internal Medicine*. Saunders Elsevier, St. Louis: 2036-47.
Rich LJ, Fabricant CG (1969): Urethral obstruction in male cats: transmission studies. *Can J Comp Med* **33**(2):164-5.
Sævik BK, Trangerud C, Ottesen N, Sørum H, Eggertsdóttir AV (2011): Causes of lower urinary tract disease in Norwegian cats. *J Feline Med Surg* **13**(6):410-17.
Segev G, Livne H, Ranen E, Lavy E (2011): Urethral obstruction in cats: predisposing factors, clinical, clinicopathological characteristics and prognosis. *J Feline Med Surg* **13**(2):101-8.
Westropp JL, Buffington CAT (2010): Lower urinary tract disorders in cats. In: Ettinger SJ, Feldman EC, editors. *Textbook of Veterinary Internal Medicine*. Saunders Elsevier, St. Louis: 2069-86.
Westropp JL, Kass PH, Buffington CA (2006): Evaluation of the effects of stress in cats with idiopathic cystitis. *Am J Vet Res* **67**(4):731-6.